Cellular Automata Computational Model of Blastocoel Roof Thinning and Matrix Assembly in *Xenopus Laevis*

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We have developed an innovative computational cellular automata (CA) model to predict how the aggregate behavior of independently acting discrete cells quantitatively affects cell patterning and extracellular matrix deposition during embryonic morphogenesis. In the blastocoel roof (BCR) of the *Xenopus laevis* embryo, thinning of multiple cell layers into two cell layers is accomplished via radial intercalation of the deep layer cells. During BCR thinning a matrix of fibronectin fibrils is assembled on the inner layer of cells. Although the general movement and patterning of the network of cells in the BCR during thinning have been observed, the underlying mechanisms responsible for cellular behavior during this process have yet to be determined. Here, we view the roof thinning process as a complex multicellular system of interacting cell motions, matrix assembly, and matrix adhesion events using a cellular automata model. A cellular automata model was developed to analyze the spatial and temporal movements of BCR cells during thinning. Based on published data and independent experimental data describing initial tissue geometry and cell numbers, cell intercalation rates, migration rates, and differential adhesion, the model predicts a morphogenetic thinning time of 4.8 hours, which closely approximates the experimentally observed time necessary for the completion of thinning. Additionally, the model predicts a temporal increase in fibronectin that is quantitatively similar to the experimentally observed increase in fibronectin during thinning. Furthermore, the model is capable of independent predictions of cell motions and patterning in the morphogenetic process, and here was used to independently predict the lateral dispersion of a patch of cells implanted in the BCR. Our discrete cell-based computational automata model has the ability to predict important characteristics of the BCR thinning process including total thinning time, fibronectin matrix assembly, and the spatial-temporal patterning of specific cells. We suggest that this CA approach to studying a complex biological patterning process has the potential to broadly impact biomedical discovery because it is 1) applicable to any biological system composed of discrete but interacting cells, 2) capable of integrating vast amounts of quantitative experimental data in a useful way to generate functional knowledge, suggest testable hypotheses, and verify experimental data, and 3) useful for the prediction of unified and consistent cellular mechanisms underlying biological functions in developmental biology.

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